UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/612,809	07/10/2000	Val C. Sheffield	UIA-029.03	8992

7590 07/16/2003

STEVE L. HIGHLANDER
FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVENUE,
SUITE 2400
AUSTIN, TX 78701

EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	20

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/612,809	SCHEFFIELD, ET AL	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a response, filed 4/24/03 as Paper No. 19, to a Notice of Non-Responsive Amendment mailed 2/17/03 as Paper No. 18. The Notice of Non-Responsive Amendment was sent on the grounds that there was no statement from Applicants' representative concerning the lack of new matter in the paper copy and CRF copy of the sequence listing submitted 2/4/03 (Paper No. 16). The response in Paper No. 19 correctly points out that such a statement was present in the submission filed 2/4/03. The examiner apologizes for missing this statement, which was located at the top of page 2 of Paper No. 16. The submission filed 2/4/03 is correct and has placed the application into sequence compliance.

Applicants' initial response to the first action on the merits (Paper No. 4, mailed 8/21/01) was filed 3/4/02 as Paper No. 6. In Paper No. 6 several claims were amended (claims 11, 15-21). A supplemental response was filed on 6/24/02 as Paper No. 9 in which several claims were amended (claims 11, 15-21). This action is in response to the amendments and arguments presented in Papers No. 6 and 9. Claims 11-24 are pending in the instant application and under consideration. This action is not final due to additional grounds of rejection made herein that were not necessitated by applicants' amendment of the claims. Any rejection of record in Paper No. 4 not addressed herein is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Claims 18-24 are drawn towards methods of identifying a compound that modulates an FKHL7 bioactivity wherein a critical element of the invention is the binding partner for FKHL7 (i.e. one must possess the binding partner for FKHL7 in order to practice the recited methods). The binding partner can be literally any compound or molecule that binds to the FKHL7 protein (e.g. small molecule, protein, peptide, DNA sequence, antibody, etc.). Thus, the claims encompass an incredibly broad genus of compounds/molecules that must satisfy the functional limitation of being able to bind FKHL7.

The instant specification asserts, based on the presence of a consensus-binding site (RTAAYA), that FKHL7 is a DNA-binding transcription factor. There is no basis provided by the instant specification, however, for one to visualize the structural/functional characteristics of a sufficient number of specific embodiments of the recited binding partners to describe the broadly claimed genus of such binding partners. Even if one accepts that FKHL7 can bind DNA, which has not been demonstrated by applicants, no specific DNA sequence has been described to which FKHL7 can bind, nor is there a basis for one of skill in the art to envision the specific sequences to which FKHL7 will bind. Similarly, it is likely that one could obtain an antibody that will specifically bind to FKHL7. There is no basis, however, for one of skill in the art to envision the specific primary sequence of the antibody. Moreover, even if one accepts that

FKHL7 can be bound by these general classes of polymers (i.e. DNA or immunoglobulins), these two general examples cannot be used to envision specific binding partners of other types (e.g. small molecule agonists or antagonists of FKHL7).

The prior art does not compensate for the deficiencies of the instant specification with regard to providing a basis for one of skill in the art to envision specific binding partners of FKHL7. There is no description in the prior art of record of *any* binding partner for FKHL7.

Given the large genus of binding partners for FKHL7 embraced by the rejected claims, and given the lack of a basis in the prior art or instant specification for envisioning specific binding partners for FKHL7, the skilled artisan would not have been able to envision a sufficient number of specific binding partners for FKHL7 to describe the broadly claimed genus of such binding partners. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the broadly claimed invention.

Response to Arguments

Applicant's arguments filed in Papers No. 6 and 9 have been fully considered but they are not persuasive. In response to a similar rejection of the claims in Paper No. 4, applicants' have essentially argued: 1) the specification has disclosed that FKHL7 possesses a consensus RTAAYA DNA-binding site shared by other DNA-binding proteins, 2) DNA could be used as a binding partner for FKHL7.

The possibility that FKHL7 is a DNA-binding protein does not provide a basis for one of skill in the art to envision even one specific embodiment of a DNA sequence to which FKHL7 will necessarily bind. Also, as indicated above, the possibility that FKHL7 will bind to DNA does not provide a basis for the skilled artisan to envision any other types of binding partners for

FKHL7 (e.g. small molecules, peptides, etc.). Therefore, the mere possibility that FKHL7 is a DNA-binding protein cannot be considered as descriptive of the broadly claimed binding partners for FKHL7 that are a critical element of the claimed invention.

Claims 14 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in Paper No. 4, mailed 8/21/01 and repeated below**.

These are genus claims encompassing any compound identified by the screening methods of claims 11 and 18, respectively. The specification fails to disclose any such compounds. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the rejected claims as one of skill in the art cannot envision the structure of any of the claimed compounds. Therefore, the specification does not describe the claimed compounds in such full, clear concise and exact terms so as to indicate that applicants had possession of these compounds at the time of filing of the present application. Thus, the written description requirement has not been satisfied.

Response to Arguments

Applicant's arguments filed in Papers No. 6 & 9 have been fully considered but they are not persuasive. The responses have essentially argued: 1) the rejected claims are product-by-process claims, 2) such claims are specifically contemplated where it is difficult or impossible to

define products by their physical characteristics (i.e. their structure), 3) product claims may include process steps that either partially or wholly define the claimed product.

At no point did the examiner state that the claims were rejected simply because they are product-by-process claims. The examiner made a cogent argument that the specification failed to disclose any specific compounds as identified by the methods of claims 11 or 18. Nor does the specification provide a basis for one of skill in the art to envision a specific compound (e.g. specific small molecule drug, peptide, RNA, etc.) that will necessarily be identified by the methods recited in claims 11 and 18. Nor do the methods steps of these claims provide a basis for one of skill in the art to envision specific embodiments of the claimed compounds (i.e. the recited methods steps do not specify some structural characteristic as to allow one of skill in the art to envision any one specific embodiment of the claimed compounds).

Claims 11-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This is a new rejection.**

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The invention is drawn toward methods of identifying compounds that modulate a human FKHL7 protein's bioactivity. The only disclosed utility for the claimed methods is to identify compounds that will modulate FKHL7 biological activity within a cell. The specification does not appear to contemplate, for example, identification of compounds that would modulate the ability of FKHL7 to be bound by an antibody. Thus, the invention is complex in that it requires an understanding of the biochemical/physiological activities associated the human FKHL7 protein within the cell.

Breadth of the claims: The rejected claims are broad in that they encompass literally any biological activity associated with the human FKHL7 protein. Claims 18-24 are slightly narrower in scope in that they require the bioactivity to be modulation of formation of an FKHL7 protein/FKHL7 binding partner complex. Yet these claims are extremely broad as well in that they encompass a very broad genus of potential partners that might functionally bind FKHL7. Thus, the great breadth of the claims add to the complexity of the invention because the skilled artisan must be able to readily determine a functional bioactivity of FKHL7 in order to practice the claimed assays.

Guidance of the specification The existence of working examples: The specification teaches that FKHL7 comprises a consensus "RTAAYA" DNA-binding domain and asserts, based upon similarity to other FKHL7-like or "forkhead" proteins, that FKHL7 is a DNA-binding transcription factor. The specification demonstrates that FKHL7 is expressed in the heart and eye during embryogenesis, and that defects in the FKHL7 gene correlate with eye defects. The specification does not teach, however, the DNA-binding substrate for FKHL7. In fact, it is never actually demonstrated that FKHL7 even binds to DNA. The specification shows

an amino acid comparison of FKHL7 to other FKHL-family proteins in Figure 2. However, the degree of similarity is not readily apparent, even within the purported helix and "wing" domains. Nor does the figure clearly teach the location and sequence of the "RTAAYA" domain within FKHL7. No other biochemical activity for FKHL7 is proposed in the specification.

State of the art: The prior art does not teach a specific biochemical activity for FKHL7. The prior art does not teach any specific binding partner for FKHL7.

Predictability of the art: The art at the time of applicants' invention did not make predictable the assignment of function to a given protein based on its primary amino acid sequence alone. The relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). Berendsen teaches that with the number of known gene sequences increasing at an accelerating rate, the quest for the structure and function of the coded proteins becomes pressing, with the obvious route to that goal being homology modeling. Yet, Berendsen teaches, that at the time of applicants invention such methods were effective for only about 25% of the proteins for which the amino acid sequence was known. For proteins with homology below 25%, the reliability was nearly zero (page 642, columns 1-2). The reference teaches that "Thus, one of the "grand challenges" of high-performance computer --predicting the structure of proteins-- acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur. It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is unpredictable as to any actual biological

activity of FKHL7. Nor would one be able to predict, for example, what binding partners FKHL7 might possess based upon its primary sequence alone.

The amount of experimentation necessary: In order to practice the claimed inventions, one of skill in the art would have to first determine the biological activities associated with the FKHL7 protein *in vivo*. While there is some indication, based upon homology, that FKHL7 may be a DNA-binding transcription factor, there is no definitive proof of such an activity. One would have to develop an assay to determine whether FKHL7 binds specifically to DNA, which would be unpredictable as evidenced by the teachings of Berendsen. Applicants have asserted in Paper No. 9 that one could perform a "global" DNA-binding and/or transcription experiment using a cell or cell-free extract comprising or expressing FKHL7 (e.g. incorporation or retention of radiolabeled nucleotides). This assertion is unsupported by any teaching of specific conditions for such an assay in the specification, particularly with regard to conditions for detecting FKHL7 transcriptional activity and/or DNA-binding activity in what would likely be a high background of non-FKHL7 related transcription or DNA sequences that do not bind FKHL7 specifically. In short, how does one make the "global" assays asserted by applicants sensitive enough to distinguish effects of a compound that are specific for FKHL7, as is required by the rejected claims? Applicants may argue that such experimentation would be routine, but that cannot be considered to be the case when there is no teaching as to the specific transcriptional and/or DNA-binding activities of FKHL7 (e.g. what sequences, if any, are bound, how tightly and to what effect). Each of these parameters would have to be determined empirically and in an unpredictable manner. Such experimentation must be considered as undue,

unpredictable experimentation. Therefore, the instant specification is not considered to be enabling for the rejected claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by applicants' amendment of the claims in Paper No. 9.**

Claim 18 is vague and indefinite in that the metes and bounds of the phrase "...indicates the test compound is a modulator of an FKHL7..." are unclear. Since only a single FKHL7 protein is recited in the claim, it is unclear what is meant by "an FKHL7". Consistent with dependent claims 22 & 23, which recite "an FKHL7 bioactivity", appears that the word "bioactivity" is missing following "FKHL7".

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
July 11, 2003